Non-Linear Spectroscopy of Chiral Molecules Achieved

Optically Active Sum Frequency Generation Demonstrated

A research group led by Y. Ron Shen has succeeded in observing characteristic non-linear spectra from chiral molecules using sum-frequency generation techniques. The new technique is sensitive to the electronic and vibrational resonances of chiral molecules and is expected to find wide applications in chemistry and biology.

Chirality, the existence of mirror-imaged "right-" and "left-handed" forms of an object, exists in all types of matter, from elementary particles and atoms to natural objects and galaxies. Molecular chirality is of particular importance because of its relevance to life on earth. More than 90% of natural biomolecules are chiral and the homochirality of these molecules is still a great mystery. Right-handed and left-handed molecules, known as enantiomers, often possess drastically different biological functions. In an extreme example, as in the notorious case of thalidomide, one could be beneficial and the other harmful. Alternatively, one enantiometer could taste sweet and the other bitter.

Molecular chirality is commonly probed by observing the rotation of polarized light: "left-handed" molecules rotate the light in one direction, "right handed" molecules rotate light in the opposite direction, and a 50/50 "racemic" mixture produces no rotation of light at all. Most common mixtures to be analyzed have a very slight excess of one isomer over the other. Commercial instruments designed to measure this and other closely related effects are installed in almost every bioscience lab. However, in general, these types of "linear" spectroscopic techniques are not sensitive enough to probe the chirality of a monolayer or thin film.

Sum frequency generation (SFG) is a "nonlinear" optical process in which two incident laser pulses at frequencies ω_1 and ω_2 interact in a sample and generate an output at their sum-frequency, $\omega_1+\omega_2$. The technique has been developed in Shen's lab as a spectroscopic tool and has been shown to be exquisitely sensitive and useful in studying surfaces and interfaces. (MSD Highlights 99-5 and 01-6). That SFG could be observed in an isotropic chiral medium was first predicted in the mid-1960's, but this prediction had not been experimentally confirmed.

By careful consideration of the non-linear light generation process in SFG, the group was able to develop the appropriate optical geometry and light polarization combinations to distinguish "chiral" and "achiral" SFG signals from chiral and racemic liquids. Because there is no "inversion symmetry" in chiral mixtures, the technique is sensitive—in contrast to conventional SFG—both to surfaces and also to the bulk. The group then obtained, for the first time, chiral SFG spectra of both electronic and vibrational resonances (see figure) from a number of liquids. Further, chiral SFG spectra of electronic resonances from a surface monolayer were also observed.

The success of demonstrating SFG spectroscopy as a sensitive technique to probe molecular chirality creates many opportunities not amenable to current techniques. It allows *in situ* studies of chiral monolayers and films, and related dynamic processes, for example, adsorption of chiral molecules on membranes. It can also be extended to microscopic studies of chiral molecules in biological samples. Research to improve the sensitivity of the technique to detect vibrational SFG spectra of chiral molecular monolayers is in progress.

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